

CLAIMS:

1. A method for modulating HIV-1 fusion cofactor expression, comprising
5 manipulating an accessory molecule on the surface of a T cell, thereby modulating HIV-
1 fusion cofactor expression.

2. The method of claim 1, wherein said accessory molecule on the surface of
a T cell is a CD28 molecule.

10 3. The method of claim 1, wherein said accessory molecule on the surface of
a T cell is a CTLA-4 molecule.

4. The method of claim 1, wherein said HIV-1 fusion cofactor is CCR5.

15 5. The method of claim 1, wherein said HIV-1 fusion cofactor expression is
down regulated.

6. The method of claim 5, wherein said HIV-1 fusion cofactor expression is
down regulated by stimulating a CD28-associated signal in the T cell.

20 7. The method of claim 6, wherein said CD28-associated signal is an
intracellular signal.

25 8. The method of claim 1, wherein said HIV-1 fusion cofactor expression is
up regulated.

9. The method of claim 8, wherein said HIV-1 fusion cofactor expression is
up regulated by inhibiting a CD28-associated signal in the T cell.

30 10. The method of claim 9, wherein said CD28-associated signal is an
intracellular signal.

11. The method of claim 1, wherein said HIV-1 fusion cofactor expression is
modulated *in vivo*.

35 12. The method of claim 1, wherein said HIV-1 fusion cofactor expression is
modulated *in vitro*.

13. The method of claim 1, wherein said accessory molecule on the surface of said T cell is manipulated by the use of an agent which interacts with said accessory molecule.

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14. The method of claim 13, wherein said agent is an antibody.

15. The method of claim 14, wherein said antibody is an anti-CD28 antibody.

10 16. The method of claim 14, wherein said antibody is an anti-CTLA-4 antibody or fragment thereof.

15 17. The method of claim 16, wherein said anti-CTLA-4 antibody binds an epitope on the CTLA-4 molecule comprising the B7-1 or B7-2 binding site.

18. The method of claim 13, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody.

20 19. The method of claim 13, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody, immobilized on a solid surface.

25 20. The method of claim 16, wherein said anti-CTLA-4 antibody is soluble.

21. A method for treating a subject having an HIV-1 infection, comprising administering to said subject an agent which stimulates a CD28-associated signal in the T cells of said subject, thereby treating said subject having an HIV-1 infection.

22. The method of claim 21, wherein said agent is an antibody.

30 23. The method of claim 22, wherein said antibody is an anti-CD28 antibody.

24. The method of claim 22, wherein said antibody is an anti-CTLA-4 antibody.

35 25. The method of claim 24, wherein said anti-CTLA-4 antibody binds an epitope on the CTLA-4 molecule comprising the B7-1 or B7-2 binding site.

26. The method of claim 21, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody.

27. The method of claim 21, wherein said agent is a combination of an anti-
5 CD28 and an anti-CD3 antibody, immobilized on a solid surface.

28. The method of claim 24, wherein said anti-CTLA-4 antibody is soluble.

29. The method of claim 21, wherein said agent is co-administered with an
10 influenza vaccine.

30. The method of claim 21, wherein said subject is suffering from chronic
HIV-1 infection.

15 31. The method of claim 21, further comprising determining the levels of
CCR5 expression in said subject.

32. The method of claim 21, further comprising determining the level of viral
load in said subject.

20 33. A method for treating a subject having an HIV-1 infection, comprising:
obtaining T cells from said subject; and
contacting said T cells with an agent which stimulates a CD28-associated
signal in said T cells of said subject, thereby treating said subject having an HIV-
1 infection.

25 34. The method of claim 33, wherein said agent is an antibody.

35. The method of claim 34, wherein said antibody is an anti-CD28 antibody.

30 36. The method of claim 34, wherein said antibody is an anti-CTLA-4
antibody or fragment thereof.

37. The method of claim 36, wherein said anti-CTLA-4 antibody binds an
35 epitope on the CTLA-4 molecule comprising the B7-1 or B7-2 binding site.

38. The method of claim 33, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody.

39. The method of claim 33, wherein said agent is a combination of an anti-5 CD28 and an anti-CD3 antibody, immobilized on a solid surface.

40. The method of claim 36, wherein said anti-CTLA-4 antibody is soluble.

41. The method of claim 33, further comprising determining the levels of10 CCR5 expression in said T cells.

42. The method of claim 33, further comprising determining the levels of viral load in said T cells.

15 43. A composition for treating HIV comprising an effective amount of an agent which downregulates an HIV-1 fusion cofactor expression.

44. The composition of claim 43, wherein said agent is coupled to a solid phase surface.

20 45. The composition of claim 43, wherein said agent is an antibody.

46. The composition of claim 45, wherein said antibody is an anti-CD28 antibody.

25 47. The composition of claim 45, wherein said antibody is an anti-CTLA-4 antibody or fragment thereof.

48. The composition of claim 47, wherein said anti-CTLA-4 antibody binds30 an epitope on the CTLA-4 molecule comprising the B7-1 or B7-2 binding site.

49. The method of claim 43, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody.

35 50. The method of claim 43, wherein said agent is a combination of an anti-CD28 and an anti-CD3 antibody, immobilized on a solid surface.

51. The method of claim 47, wherein said anti-CTLA-4 antibody is soluble.

52. The composition of claim 43, further comprising an agent that provides a primary activation signal to the T cell.

5 53. The composition of claim 52, wherein said agent that provides a primary activation signal to the T cell is an anti-CD3 antibody.

10 54. A method for identifying an agent that modulates the expression of an HIV-1 fusion cofactor, comprising:
providing a T cell expressing a cell surface receptor which binds a costimulatory molecule;
stimulating a signal transduction pathway associated with said receptor;
contacting said T cell with said agent; and
determining the levels of expression of said HIV-1 fusion cofactor,
15 thereby identifying an agent that modulates the expression of an HIV-1 fusion cofactor.

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